

Dietary Exposures to Selected Metals and Pesticides

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Average daily dietary exposures to 11 contaminants were estimated for approximately 120,000 U.S. adults by combining data on annual diet, as measured by a food frequency questionnaire, with contaminant residue data for table-ready foods that were collected as part of the annual U.S. Food and Drug Administration Total Diet Study. The contaminants included in the analysis were four heavy metals (arsenic, cadmium, lead, mercury), three organophosphate pesticides (chlorpyrifos, diazinon, malathion), and four organochlorine pesticides (dieldrin, *p,p'*-DDE, lindane, heptachlor epoxide). Dietary exposures to these contaminants were highly variable among individuals, spanning two to three orders of magnitude. Intraindividual exposures to the metals, organophosphates, and organochlorines were estimated to be strongly correlated; Pearson's correlation coefficients ranged from 0.28 for lindane:dieldrin to 0.84 for lead:mercury. For some of the compounds (e.g., arsenic and dieldrin), a substantial fraction of the population was estimated to have dietary intakes in excess of health-based standards established by the EPA. Before use for risk assessment or epidemiologic purposes, however, the validity of the exposure estimates must be evaluated by comparison with biological indicators of chronic exposure. Because of their low detection rate in table-ready foods, the estimated distributions of exposures for dieldrin, *p,p'*-DDE, heptachlor epoxide, lindane, diazinon, and chlorpyrifos were found to be sensitive to assumed values for nondetect samples. Reliable estimates of the population distribution of dietary exposures to most other contaminants cannot be made currently, due to their low rate of detection in table-ready foods. Monitoring programs that use more sensitive study designs and population-based assessments for other subpopulations should be a priority for future research. **Key words:** diet, epidemiology, exposure assessment, food frequency questionnaire, heavy metals, pesticides, Total Diet Study, uncertainty. *Environ Health Perspect* 104:202–209 (1996)

The consumption of foods containing environmental contaminants is a potentially significant source of human exposure to numerous metals and pesticides (1–3). The U.S. Environmental Protection Agency (EPA), Food and Drug Administration (FDA), and Department of Agriculture (USDA) are responsible for ensuring the safety of the U.S. food supply. These agencies, in conjunction with state and local public health departments, meet this obligation by conducting various food-contaminant monitoring programs and assessment activities (2,4,5). Nevertheless, current assessments of dietary exposures to food contaminants for the U.S. population are limited by incomplete information on diets of individuals and residue levels in foods (1,6). Little is known about the variability of dietary exposures among individuals, and hence health risks, that arises from different diets or different contaminant levels in foods. The degree of uncertainty about the dietary intake estimates published by the EPA and FDA is also poorly understood. Consideration of variability and uncertainty is a fundamental component of effective environmental health management strategies (7) and is a key element of a federal bill designed to standardize exposure and risk assessments (8).

For these reasons, it is important to understand the magnitude, sources, and

variability of dietary exposures to environmental contaminants experienced by members of the population, the precision of dietary exposure estimates possible from existing data, and the prospect of using dietary exposures in epidemiologic studies designed to characterize the human health effects of specific compounds or classes of compounds. In this paper, we present the results of an investigation of these issues in relation to the dietary intakes of 11 food contaminants estimated for approximately 120,000 U.S. adults.

Methods

Dietary exposures to arsenic, cadmium, lead, mercury, chlorpyrifos, diazinon, malathion, *p,p'*-DDE, dieldrin, heptachlor epoxide, and lindane were estimated for a large population of adults in the United States by matching food consumption data collected as part of the Nurses' Health Study (NHS) and the Health Professionals' Follow-up Study (HPFS) with residue data for table-ready foods collected as part of the FDA Total Diet Study. These chemicals were selected based on a relative abundance of residue data and because they represent three classes of ubiquitous environmental contaminants: toxic metals, organophosphate pesticides, and organochlorine pesticides.

The NHS and HPFS are prospective epidemiologic studies that originally included 121,700 female registered nurses who were 30–55 years of age in 1976 (9) and 51,529 male health professionals who were 40–75 years of age in 1986 (10), respectively. The NHS and HPFS participants have been followed up every 4 years with a mailed questionnaire that updates food consumption patterns, major illnesses, and other information (9,10). Beginning in 1986, food consumption patterns were measured using a self-administered, 131-item, semiquantitative food frequency questionnaire of the previous year's diet (11). Food frequency questionnaires are designed to measure long-term average diet rather than to provide a precise estimate of short-term consumption habits (12,13).

The study population consisted of members of the NHS and HPFS cohorts who returned diet questionnaires in 1986 and/or 1990. Individuals who reported daily energy intakes outside the range of 800–4200 kcal for men and 700–3400 kcal for women or who left 70 or more of the food items blank were excluded from the analysis because their diet questionnaire responses were believed to be unreliable. The total number of food consumption records available for this study was 75,542 (1,724 excluded) and 78,882 (1,454 excluded) from 1986 and 1990, respectively, for the NHS cohort and 49,934 (1,396 excluded) and 38,075 (770 excluded) from 1986 and 1990, respectively, for the HPFS cohort.

The Total Diet Study is a market basket survey conducted annually by the FDA in which levels of selected elements, pesticides, radionuclides, and industrial chemicals are measured in 234 food items (14). Identical food items are purchased in three cities

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within each of four geographic regions and sent to an FDA laboratory in Kansas City, where the three samples of each food item from each region are composited, prepared for consumption, and subsequently analyzed for contaminant and nutrient levels (15). This design yields four residue values (one for each region) for each of the 234 foods each year. The FDA reports residue concentrations in one of three ways: those that exceed the limit of quantification (LOQ) are quantitatively reported, those below the LOQ but above the limit of detection (LOD) are quantitatively reported and identified as "trace," and those that are below the LOD are reported as "not detected" (16).

We assumed that the mean concentration for a given contaminant in each of the 131 foods listed on the food frequency questionnaire represented the average concentration of the contaminant that a person would be exposed to after repeated consumption of portions of that food over a year. Residue data for individual samples collected from the 1986–1991 Total Diet Studies were obtained from Technical Assessment Systems, Inc., an EPA contractor working on dietary exposure issues (17). Mean residue levels in each of the 234 foods were estimated by contaminant from all of the concentrations measured over the entire 6-year period and were subsequently matched to the foods on the diet questionnaire. The standard error of the mean was also computed and was assumed to be a measure of the uncertainty about the true but unknown mean residue level. A statistical analysis of the foods for which all the samples ($n = 24$) were above the LOD indicated that the contaminant levels were approximately lognormally distributed. Therefore, the contaminant concentrations in all foods were assumed to follow a lognormal distribution for purposes of estimating the mean and standard error of the residue levels. One of three methods was used to characterize the uncertainty about the mean residue concentrations based on the fraction of food samples that contained detectable residue concentrations.

For foods for which all the sample concentrations were greater than the LOD, the mean concentration was computed directly, and the variance of the estimated mean residue concentration (the square of the standard error) was computed as described by Gilbert (18) for lognormally distributed random variables. This method takes account of the fact that the distribution of sample means obtained from repeated samples of small size from a skewed distribution will be asymmetric.

For foods for which at least 50% but not all the sample concentrations were greater than the LOD ($12 \leq n \leq 23$), the maximum likelihood estimation method of Cohen, as described by Haas and Scheff (19), was used to estimate the mean and variance of the log-transformed distributions. In this method, the mean and variance of the log-transformed values of the measured data are used to estimate the parameters of the entire distribution based on the LOD and the fraction of samples below the LOD. The parameters of the lognormal distribution were then estimated from the maximum likelihood estimates of the parameters of the log-transformed data set.

For foods for which at least one but less than 50% of the sample values were above the LOD, the mean residue concentration was computed as the weighted sum of the detected concentrations and one-half the LOD. The FDA does not directly report LODs; therefore, the LOD for each contaminant was inferred from the residue data as described below. Among all the foods for which at least one sample contained a detectable amount of residue, the minimum trace amount of each chemical (i.e., the LOD) was found to be approximately 10% of the LOQ. Therefore, for foods for which less than half the samples contained detectable contaminant levels, concentrations in food samples containing levels less than the LOD were set to 5% of the LOQ (i.e., 1/2 LOD), which is a common method of treating undetected sample values. For these foods, the geometric standard deviation (GSD) of the residue concentrations was assumed to be 2.0 for metals and 3.0 for pesticides. These assumptions were based on an analysis of the GSDs of residue levels computed for foods with complete data sets ($n = 24$), which showed that the mean GSDs for metals and pesticides were 1.50 ($n = 65$ foods) and 2.24 ($n = 18$ foods), respectively. The mean GSDs for metals and pesticides were found to be highly significantly different ($p < 0.0001$) by a Wilcoxon rank sum test. The 90th percentiles of the metal and pesticide GSDs were 1.88 and 2.91, respectively, approximations of which (2.0 and 3.0) were used to compute the variance of the mean concentration as described above. We used the 90th percentiles of the metal and pesticide GSDs to provide some assurance that the uncertainty about the mean residue values was not underestimated for these foods. The sensitivity of the results to these choices was later tested.

The 234 Total Diet Study foods were matched with the 131 foods on the diet

questionnaire by food item and with an additional 52 ingredient items that are used in standard recipes to estimate exposures from foods such as homemade breads and sweets that may be reported as frequently consumed. The residue concentration for foods on the questionnaire that did not match with a Total Diet Study food were set to 1/2 LOD for each contaminant. In these cases, the uncertainty about the mean concentration was characterized as the standard deviation of a uniform random variable ranging from 0 to 1/2 LOD. Exposures due to consumption of contaminants in water were not considered because the Total Diet Study does not measure contaminant levels in tap water, which was assumed to be the primary source of water for the general population.

The number of Total Diet Study foods that contained a detectable residue concentration in at least one sample, the analytical LOQs, the number of Total Diet Study foods with mean residue concentrations below the LOQ, and the results of the matching procedure are summarized by contaminant in Table 1. Total daily average contaminant exposures from food ($\mu\text{g/day}$) for individuals were computed as the sum of the product of the mean residue amount per serving size ($\mu\text{g/serving}$) and the average daily consumption rate (servings/day) of each food reported by each individual. The mean and standard error of the amount of contaminant per serving size were computed from the corresponding concentrations using standard serving sizes (g) employed in all studies that use the NHS and HPFS food frequency questionnaires (20).

Table 1. Summary of Total Diet Study (TDS) limits of quantification (LOQ), number of TDS food items with at least one sample with a detectable residue concentration (N_{TDS}), number of TDS food items with mean residue concentration below the LOQ, and the number of TDS foods directly matched to the 183 food and ingredient items on the diet questionnaire (FFQ)

Compound	LOQ (ppb)	N_{TDS}	$N_{\text{TDS}} < \text{LOQ}$	TDS-FFQ match	
				Direct	No match
Arsenic	20	146	97	106	77
Cadmium	10	203	105	147	36
Lead	20	180	32	133	50
Mercury	10	210	204	153	30
Chlorpyrifos	3	111	87	90	93
Diazinon	2	122	84	104	79
Malathion	3	97	31	76	107
<i>p,p'</i> -DDE	2	127	82	96	87
Dieldrin	2	89	76	69	114
Heptachlor epoxide	2	55	52	45	138
Lindane	1	61	42	58	125

^aFrom Tomerlin et al. (17).

Precision of Estimated Contaminant Exposures

The precision of the estimated contaminant exposures was investigated by quantifying the uncertainty about the residue and food consumption components of dietary exposure and using analytical methods to propagate the uncertainty about the inputs through to the estimated exposures. Uncertainty about food consumption rates was estimated by using data collected during a validation study of the 131-item diet questionnaire (11,21). In 1986, 127 participants in the HPFS completed food frequency questionnaires 1 year apart and completed two 1-week diet records 6 months apart during the intervening year. The mean daily consumption of each food was computed from the diet records for each participant and was used as the true measure of average daily food-specific consumption over the year. The daily average consumption rate reported on the second questionnaire for each food, which is designed to represent consumption over the preceding year, was regressed against the corresponding mean consumption rate determined from the diet records:

$$DR_i = FFQ_i + \varepsilon \quad (1)$$

where i = number of subjects; 1,...,127; DR_i = mean consumption rate estimated from the diet records of person i (servings/day); FFQ_i = mean consumption rate reported on the food frequency questionnaire by person i (servings/day); ε = a normally distributed random variable with mean zero and standard deviation of the regression residuals, the root mean square error (RMSE; servings/day). The RMSE for each food was used to characterize the measurement error or uncertainty about the true daily consumption rate of the food

relative to that reported on the diet questionnaire.

The uncertainty about the dietary intake of the 11 contaminants for a hypothetical individual who consumed the mean amount of each of the 131 foods was calculated by decomposing the dietary exposure variance into the absolute and relative contributions of the variances of the food-specific consumption and residue values (22); the covariance between the consumption and residue values was assumed to be negligible. For example, the variance (i.e., uncertainty) of the mean arsenic exposure (s^2_{As}) was computed as follows:

$$s^2_{As} = \sum_{j=1}^{131} \left[\mu_{I,j}^2 \cdot s_{C,j}^2 + \mu_{C,j}^2 \cdot s_{I,j}^2 \right] \quad (2)$$

where, $\mu_{I,j}^2$ = square of the mean daily consumption (I) of food j (servings/day)²; $s_{C,j}^2$ = variance of the mean As concentration (C) in food j (μg/serving)²; $\mu_{C,j}^2$ = square of the mean As concentration (C) in food j (μg/serving)²; $s_{I,j}^2$ = square of the RMSE of the consumption estimate (I) from the regression equation for food j (serving/day)².

Table 2. Summary of estimated dietary exposure (μg/day) distributions for 78,882 adult females and 38,075 males in 1990^a

Gender	Chemical	Mean	GM	GSD	Min	Max	Fit (r^2)
Female	Arsenic	50.6	39.7	2.09	1.01	1081.0	0.972
	Cadmium	18.5	17.4	1.42	2.62	104.2	0.998
	Lead	14.9	13.6	1.51	2.07	163.5	0.999
	Mercury	8.2	6.8	1.87	0.37	203.5	0.985
	Chlorpyrifos	0.8	0.8	1.47	0.12	5.6	0.998
	Diazinon	0.5	0.5	1.36	0.10	2.0	0.998
	Malathion	5.5	4.7	1.77	0.15	50.8	0.994
	<i>p,p'</i> -DDE	1.2	1.0	1.59	0.15	16.7	0.958
	Dieldrin	0.5	0.5	1.46	0.08	4.3	0.998
	Heptachlor epoxide	0.3	0.3	1.35	0.05	1.0	0.994
	Lindane	0.2	0.2	1.51	0.03	3.2	0.986
Male	Arsenic	58.5	45.7	2.10	0.21	1276.0	0.968
	Cadmium	19.3	18.2	1.44	0.91	162.3	0.999
	Lead	14.8	13.4	1.54	0.59	160.3	0.999
	Mercury	8.6	6.9	1.92	0.22	165.7	0.991
	Chlorpyrifos	0.9	0.8	1.51	0.03	6.0	0.997
	Diazinon	0.5	0.5	1.39	0.02	2.7	0.998
	Malathion	6.1	5.2	1.80	0.03	56.9	0.996
	<i>p,p'</i> -DDE	1.2	1.0	1.65	0.02	16.9	0.947
	Dieldrin	0.5	0.5	1.47	0.02	4.0	0.998
	Heptachlor epoxide	0.3	0.3	1.38	0.02	1.2	0.998
	Lindane	0.2	0.2	1.55	0.01	2.9	0.989

^aMean, arithmetic mean; GM, geometric mean; GSD, geometric standard deviation; Min, minimum; Max, maximum; Fit, r^2 from regressing natural-log transformed data on corresponding z-scores.

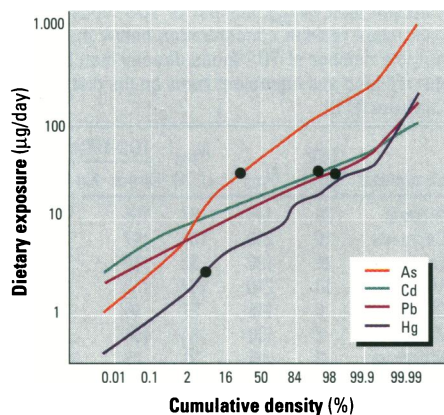


Figure 1. Distributions of dietary exposures to 4 metals estimated for 78,882 adult females in 1990. Circles indicate intakes estimated for a typical adult female by previous researchers (23).

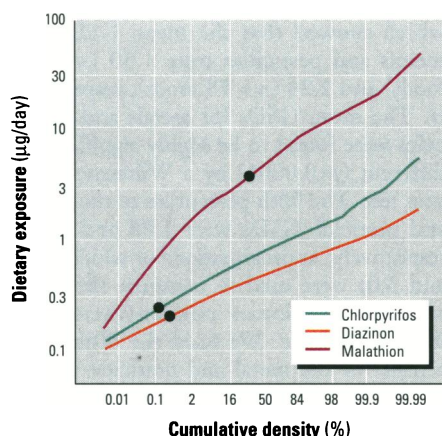


Figure 2. Distributions of dietary exposures to 3 organophosphate pesticides estimated for 78,882 adult females in 1990. Circles indicate intakes estimated for a typical adult female by previous researchers (34).

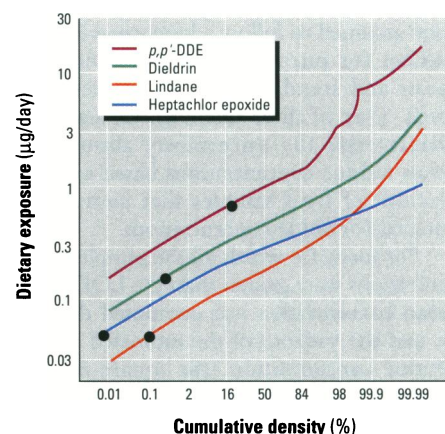


Figure 3. Distributions of dietary exposures to 4 organochlorine pesticides estimated for 78,882 adult females in 1990. Circles indicate intakes estimated for a typical adult female by previous researchers (34).

Results

The distributions of dietary exposures to 11 food contaminants estimated for NHS participants who completed valid diet questionnaires in 1990 are summarized in Figures 1–3, and summary statistics for both the 1990 NHS and HPFS participants (1990 responses) are presented in Table 2. All of the distributions were approximately lognormally distributed; the r^2 between the natural log of the estimated exposures and the corresponding z -scores was greater than 0.95 for all (≥ 0.99 for most) cohort-chemical combinations. Differences between intakes estimated for the male and female cohorts were small. Summary statistics of the estimated exposure distributions based on the 1986 diet questionnaires from both males and females were within 3% of the values developed from the 1990 food consumption data. Individual dietary exposures to each compound were estimated to range over two to three orders of magnitude.

Pearson correlation coefficients between predicted exposures to the 11 contaminants were estimated from the 1990 results for the NHS and HPFS participants (Table 3). Because of the large sample size for each cohort, all of the estimated correlation coefficients were highly statistically significant. There was little difference between the correlation coefficients estimated for males and females. Pairwise correlation coefficients among all of the metals were at least 0.4 and reached as high as 0.83 between arsenic and mercury, most likely because the highest concentrations of both chemicals are found in fish. Pairwise correlation coefficients between contaminants in the respective pesticide groups ranged from 0.3 to 0.72, indicating that an individual highly exposed to one of these compounds is likely to also be highly exposed to others.

Using the error propagation technique described previously, the uncertainty about the mean daily dietary exposure to arsenic, cadmium, p,p' -DDE, lead, malathion, and mercury was estimated for a hypothetical member of the 1986 HPFS cohort who consumes the mean amount of each food per day reported on the diet questionnaires. The other five chemicals (chlorpyrifos, diazinon, dieldrin, lindane and heptachlor epoxide) were excluded because, as described later, the population exposures for these chemicals were dominated by food items for which the majority of samples contained residue concentrations below the LOD. Therefore, we believe that uncertainty about dietary exposures to those chemicals is dominated by a lack of knowledge about their true average concentrations in food.

The coefficient of variation (CV), computed as the square root of the estimated variance (Eq. 2) for a contaminant divided by the mean exposure for the contaminant, ranged from 21% for cadmium to 49% for malathion, indicating that the exposures to these chemicals estimated for a given individual may be accurate to within approximately a factor of 2 (Table 4). Lack of data about the actual amount of food consumed accounted for at least 80% of the total uncertainty for arsenic, cadmium, mercury, and malathion. Individual food items contributing most to uncertainty for these chemicals were, for arsenic, fish, canned tuna, and shrimp; for cadmium, spinach, coffee, lettuce, nuts, potatoes, and assorted beverages; for mercury, canned tuna and other fish; and for malathion, white and dark bread. The source of uncertainty about exposures to p,p' -DDE and lead was approximately equally split between a lack of data about consumption rates and residue levels. The foods contributing most to uncertainty about the p,p' -DDE estimate were whole milk, spinach, and beef,

while those for lead were canned tuna, skim milk, peaches, coffee, and white wine.

To investigate the uncertainty about the estimated mean daily exposure to these chemicals among the study population, uncertainty about food consumption was assumed to be negligible (reflecting the large sample from which the average consumption rate of each food item was obtained). In this scenario, the coefficient of variation ranged from 7% for arsenic to 30% for lead (Table 4) and varied inversely with respect to the percentage of the population exposure composed of foods for which at least half of the Total Diet Study samples were above the LOD.

Discussion

We assessed average daily dietary exposures to 11 food contaminants for approximately 120,000 U.S. adult males and females. Because of the large sample size and geographic diversity of the study population, we believe the results are generalizable to the majority of the U.S. adult population. However, because of the age and occupational restrictions on admission to the NHS and HPFS cohorts and the potential for correlations between demographics and diet, the results may not be representative of dietary exposures to members of certain age, ethnic, socioeconomic, and other subpopulations.

The residue levels used to estimate the dietary exposures presented here were based solely on the results of the 1986–1991 Total Diet Studies. While information from more recent Total Diet Studies were not used due to our inability to easily access the data, summary reports indicate that contaminant levels in food have been relatively constant in recent years (5). The Total Diet Study data represent the best available measures of contaminant levels in table-ready foods; however, they are subject

Table 3. Estimated Pearson correlation coefficients between dietary intakes of 11 food contaminants for 78,882 adult females (upper right) and 38,075 adult males (lower left)^a

	As	Cd	Pb	Hg	Ch	Dz	Mal	DDE	Diel	HCH	Hep
As		0.39	0.69	0.83	0.24	0.31	0.08	0.23	0.33	0.05	0.24
Cd	0.36		0.60	0.40	0.54	0.69	0.39	0.55	0.64	0.31	0.59
Pb	0.71	0.57		0.82	0.41	0.52	0.20	0.40	0.48	0.26	0.52
Hg	0.84	0.37	0.84		0.26	0.32	0.12	0.27	0.30	0.07	0.28
Ch	0.22	0.55	0.40	0.24		0.69	0.36	0.35	0.51	0.27	0.60
Dz	0.31	0.70	0.50	0.30	0.68		0.48	0.51	0.62	0.40	0.79
Mal	0.06	0.41	0.17	0.09	0.36	0.47		0.25	0.27	0.21	0.36
DDE	0.14	0.50	0.32	0.17	0.30	0.46	0.23		0.52	0.35	0.62
Diel	0.27	0.68	0.45	0.25	0.54	0.63	0.30	0.52		0.28	0.69
HCH	0.04	0.34	0.25	0.06	0.28	0.43	0.22	0.39	0.35		0.45
Hep	0.19	0.60	0.46	0.21	0.58	0.77	0.36	0.63	0.72	0.51	

Abbreviations: Ch, chlorpyrifos; Dz, diazinon; Mal, malathion; DDE, p,p' -DDE; Diel, dieldrin; HCH, lindane (hexachlorocyclohexane); Hep, heptachlor epoxide.

^aCorrelation coefficients between the contaminants comprising the metal, organophosphate and organochlorine groups are shaded and all coefficients greater than 0.5 are in bold type.

Table 4. Summary of uncertainty about estimated dietary exposure to six contaminants in food for a person who consumes the mean amount of each food reported on the 1986 HPFS diet questionnaires^a

	CV (%)	% Residue	% Consumption	CV* (%)
Arsenic	41	3	97	7
Cadmium	21	19	81	9
p,p' -DDE	35	34	66	20
Lead	43	50	50	30
Malathion	49	4	96	10
Mercury	44	5	95	9

^aEstimated coefficient of variation (CV) about average daily intake ($\mu\text{g/day}$); the relative contribution of uncertainty about mean residue concentrations and food consumption patterns; and the CV assuming uncertainty about food consumption is negligible (CV*).

to the limitations of relatively small sample sizes ($n = 4$ for each food item each year, based on a composite of three items per sample). In the Total Diet Study, samples are obtained from grocery stores and thus may not be representative of homegrown foods or those available at specialty retail outlets such as farmers' markets and organic grocers. We assumed that any systematic regional or seasonal effects on contaminants levels in food and individual diets were negligible. In reality, seasonal and regional variability of food consumption rates, possibly due to availability and prices, and residue levels, from nonuniform pesticide application rates, for example, may be important contributors to interindividual variability of dietary exposures. Currently, there are insufficient data to investigate the veracity of the simplifying assumptions made in our analysis. However, our estimates likely underestimate the actual variability of dietary exposures to these chemicals among U.S. citizens, as well as the degree of uncertainty about the true exposure distributions.

Nevertheless, this work is believed to be the first attempt to characterize the interindividual variability of exposures to contaminants in food. Numerous other researchers, primarily affiliated with the FDA, have estimated typical intakes of the 11 contaminants considered here. The dietary exposures estimated for a typical female adult by previous researchers are indicated in Figures 1–3. The typical intake for arsenic estimated elsewhere is well within the distribution estimated from the diet questionnaire (23). The cadmium and lead intakes estimated by Gunderson (23) lie in the upper tail of the NHS distribution, whereas the mercury estimate is equivalent to the 9th percentile of the NHS distribution. In general, typical pesticide exposures estimated by the FDA fall well into the lower tail of the corresponding NHS distribution, except for the malathion and *p,p'*-DDE estimates, which correspond to the 37th and 21st percentiles of the estimated distribution, respectively.

Differences between the typical estimates made previously and those based on the questionnaire are most likely due to the treatment of residue values that were not detected; the FDA estimates were based solely on foods for which trace or quantifiable residue concentrations were measured (i.e., nondetection samples were set to zero), while in our analysis, residue levels for food samples that contained nondetectable concentrations were set to $1/2$ LOD. Comparing the typical pesticide intakes estimated by the FDA to the maximum values obtained from the distribution estimated for the 1990 NHS cohort shows

that the combination of using average food consumption patterns for a subpopulation and setting nondetection values to zero may underestimate exposures for some members of the population by a factor of 10–60.

Sensitivity of Results

The sensitivity of the predicted exposure distributions to treatment of residue samples below the LOD was investigated by estimating the distributions for the 1990 NHS respondents under two cases in addition to the current estimates: 1) nondetect samples set to zero and 2) nondetect samples set to the LOD (Fig. 4). The EPA Integrated Risk Information System (IRIS) was queried on 8 November 1994 for human health-based exposure standards for the 11 chemicals included in our analysis. We retrieved cancer potency values [q_1^* ($\text{mg/kg/day})^{-1}$] for ingestion of compounds treated by the EPA as carcinogenic in humans and reference doses (RfD; mg/kg/day) for ingestion of the noncarcinogens (Table 5). Exposures exceeding the RfD and the level estimated to produce an excess lifetime cancer risk (ELCR) of 10^{-4} are compared to the predicted dietary exposure predictions in Figure 4. The original exposure estimates ($\mu\text{g/day}$) were converted to units of $\mu\text{g/kg/day}$ by assuming a uniform body weight of 65 kg for adult females.

The estimated exposure distributions for cadmium, lead, arsenic, mercury, and malathion were relatively insensitive to different assumptions about the true concentration in foods with residues below the LOD. Note the divergence of the lower end of the predicted mercury distributions due to diets primarily composed of foods containing mercury levels below the LOD. Assuming inorganic arsenic accounts for 10% of all arsenic in foods (24), a substantial fraction of the population was estimated to have dietary exposures to inorganic arsenic that exceed the RfD (13% of the population) and a 10^{-4} ELCR (80%). The validity of this model result must be evaluated by future research of arsenic speciation in different foods.

The predicted dietary exposure distributions for the remaining six contaminants were sensitive to the treatment of nondetect residue samples (Fig. 4). For example, median exposure estimates ranged by a factor of 2 for diazinon to a factor of 10 for heptachlor epoxide. This degree of uncertainty is of apparent little consequence in some cases, such as chlorpyrifos, where all predicted exposures are well below the health-based RfD. In contrast, the fraction of the population predicted to be exposed to dieldrin at levels estimated to produce

an ELCR greater than 10^{-4} ranged from approximately 10% to 85% over the three cases, while the fraction of estimated heptachlor epoxide exposures above the RfD and equivalent to an ELCR greater than 10^{-4} ranged from 0 to approximately 20%. These results indicate that the number of individuals predicted to bear health risks above what may be considered a tolerable level can change by tens of millions depending on assumptions made about the contaminant concentrations in foods with residues below the LOD. This uncertainty can only be resolved by additional monitoring efforts that use a more sensitive design, which should be a priority for future research.

The sensitivity of the error analysis results to assumptions made regarding the uncertainty about mean residue levels in food items for which less than half of the samples were above the LOD was also investigated. The error analysis was repeated after estimating the variance of the mean residue concentration in food items for which less than half of the samples were above the LOD based on the mean GSD rather than the 90th percentile GSD for metals and pesticides, respectively. The results were found to be virtually identical to those presented above.

Excluding water from the analysis is not expected to have a substantial impact on our results because of the generally low levels of contaminants in drinking water. For example, arsenic is typically present in drinking water at approximately $2 \mu\text{g/l}$ (25), which at a consumption rate of 2 l/day would increase the mean arsenic exposure of approximately $55 \mu\text{g/day}$ by about 7%. Similar results were estimated for cadmium, mercury, and the pesticides based on typical tap water concentrations published in the literature (26–29). The EPA (30) estimated that drinking water supplies used by 99% of the U.S. population contained lead levels less than $5 \mu\text{g/l}$. Assuming a typical lead concentration of $3 \mu\text{g/l}$, water consumption may account for an additional $6 \mu\text{g/day}$ of dietary exposure, nearly 40% of the $15 \mu\text{g/day}$ estimated from food alone.

Health risk assessments of environmental contaminants are typically based on exposure or dose rates expressed on a body weight basis (e.g., $\mu\text{g contaminant/kg body weight/day}$). The exposure rates presented here were expressed on a mass per day basis ($\mu\text{g/day}$), which may limit their utility for use in risk assessments due to concerns about correlations between food consumption and body weight. However, Willett et al. (31) found that neither height nor body weight were significantly correlated with

total caloric intake among a group of 194 adult women who completed four 1-week diet records over a year. Physical activity is a major determinant of energy intake, and metabolic efficiency may be a minor determinant (32). Investigations of potential correlations among these factors, body weight, and the types of foods consumed by individuals are likely to yield results that would be more useful for environmental risk assessments.

Determinants of Dietary Exposure

To better understand the sources of dietary exposures to the contaminants considered in our analysis, we determined the relative contributions of the 131 food items on the food frequency questionnaire to the mean exposure estimated for individuals composing the upper and lower deciles of the exposure distributions estimated for the NHS participants who completed valid diet questionnaires in 1990.

For individuals in the first decile of the arsenic exposure distribution, canned tuna (28%), chicken (11%), and white rice (10%) were estimated to be the principal contributors to exposure, while arsenic exposures for individuals at the upper end of the distribution were due to frequent consumption of fish (92%). Cadmium exposures for individuals at either end of the estimated exposure distribution were due to consumption of liver (10%), potatoes (8%), spinach (8%), iceberg lettuce (7%), and pasta (5%), with no single food making a particularly large contribution. For lead, canned tuna was estimated to be the principal contributor to the average exposure among individuals in the first (11%) and tenth (34%) deciles; exposures in the upper decile were marked by more frequent consumption of canned tuna and other fish. Dietary exposures to mercury at the upper end of the estimated distribution were dominated by consumption of fish products (87%), principally canned tuna (65%).

Table 5. IRIS exposure standards for the 11 chemicals analyzed

Chemical	RfD ($\mu\text{g/kg/day}$)	q_1^* ($\mu\text{g/kg/day}$) ⁻¹
Arsenic (inorganic)	0.3	0.00175
Cadmium	1.0	—
Mercury	(under review)	—
Lead	—	—
Chlorpyrifos	3.0	—
Diazinon	(under review)	—
Malathion	20.0	—
<i>p,p'</i> -DDE	—	0.00034
Dieldrin	0.05	0.016
Heptachlor epoxide	0.013	0.00091
Lindane	0.3	—

Abbreviations: IRIS, EPA Integrated Risk Information System; RfD, reference dose.

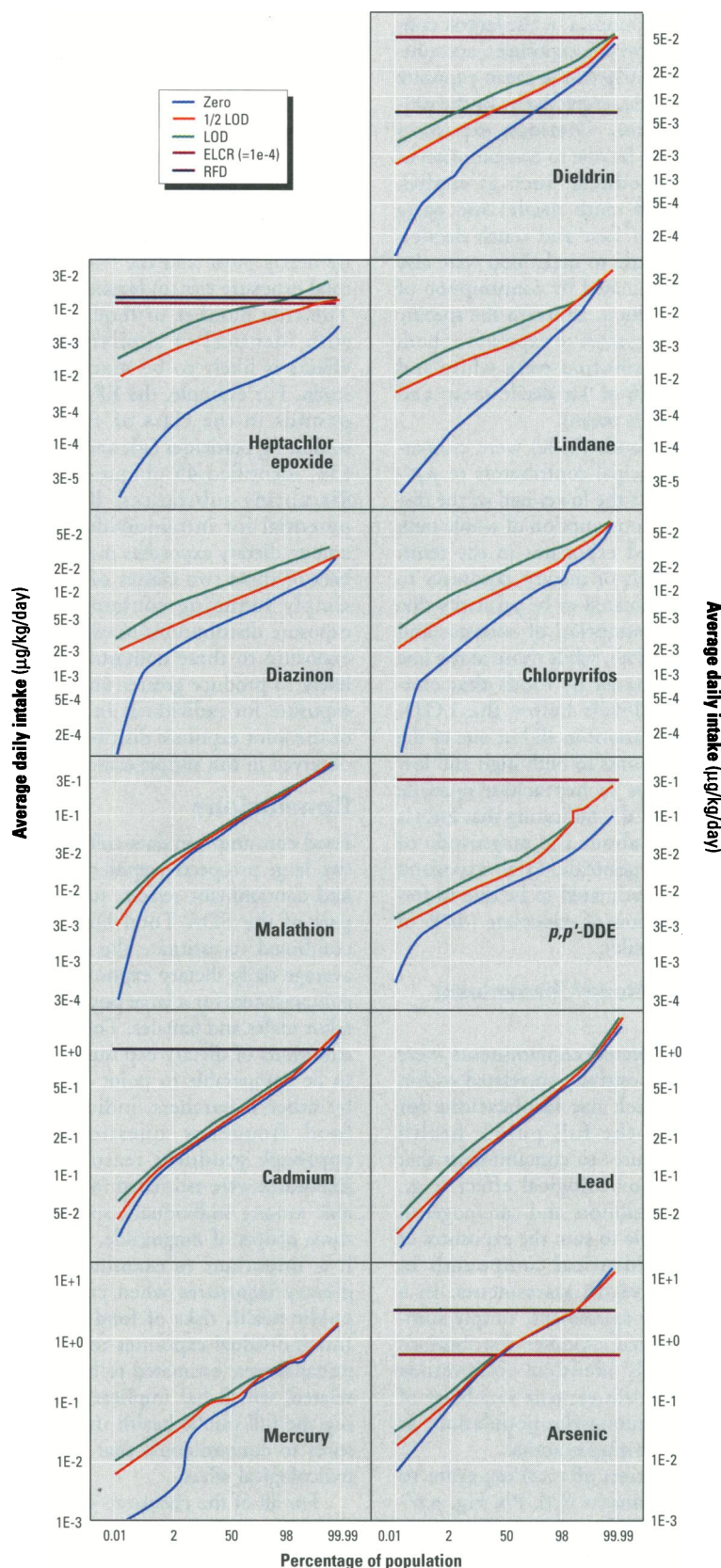


Figure 4. Estimated average daily contaminant intakes from food among 78,882 adult females in 1990 under 3 different assumptions about the true mean contaminant concentration in foods containing amounts below the Total Diet Study limit of detection (LOD). Average daily intakes that correspond to an excess lifetime cancer risk (ELCR) of 10^{-4} and the reference dose (RfD) for noncancer effects established by the EPA are shown for purposes of comparison.

Apples were found to be the largest contributor to chlorpyrifos exposures, accounting for 9% and 36% of the mean exposure for the tenth decile, respectively, of the estimated distribution. Diazinon exposures were estimated to be due to consumption of wheat-based products, such as english muffins (11% of tenth decile) and pasta (9% of mean for first and tenth decile). Estimated exposures to malathion were also found to be dominated by consumption of wheat-based products, although the specific items contributing most to exposure at both ends of the distribution were white and dark breads (24% of 1st decile mean and 65% of 10th decile mean).

Beef-related foods (15%) were estimated to be the principal contributors to *p,p'*-DDE exposures at the lower end of the distribution, while consumption of whole milk (42%) dominated exposures in the tenth decile. High levels of dietary exposures to dieldrin were estimated to be primarily due to frequent consumption of summer and winter squash (38%), while those at the low end were dominated by foods that contained residue levels below the LOD. Residue concentrations in all but one of the principal contributors to both high and low dietary exposures to heptachlor epoxide were set to 1/2 LOD, indicating that little is actually known about the magnitude of exposure to this pesticide. High exposures to lindane were estimated to be due to frequent consumption of chocolate (48% of mean for 10th decile).

Correlations among Contaminant Exposures

Exposures to selected contaminants were estimated to be positively correlated within individuals, which has implications for understanding the full public health impacts of exposures to contaminants that have the same toxicological effect (e.g., cholinesterase inhibitors and carcinogens). It seems reasonable to sum the exposures of toxicologically identical compounds in environmental health assessments. In a population-based assessment, simply summing the correlated exposure distributions of toxicologically identical compounds would underestimate the true variability of total exposure among the population, as shown in the following example.

The distribution of total exposure to the seven contaminants (Cd, Pb, Hg, *p,p'*-DDE, dieldrin, lindane, heptachlor epoxide) included in our analysis that have been identified as hormonal agonists (33) was simulated for the 1990 NHS cohort using the summary statistics of the lognormal distributions, shown in Table 2, and the correlation coefficients, presented in Table

3. Simulations consisting of 10,000 trials were conducted with and without correlations among contaminant-specific exposures for individuals. When correlations were not considered, the standard deviation (10.9 µg/day) of total exposure among individuals underestimated the standard deviation (16.0 µg/day) from the simulation that did consider correlated exposures by nearly 50%, and the 95th percentile of total exposure was underestimated by 15%. The true number of food contaminants with identical or similar toxicological effects is likely to be much greater than seven. For example, the EPA lists 34 compounds in the class of cholinesterase-inhibiting pesticides (4), and Colborn et al. (33) identified 45 ubiquitous endocrine-disrupting substances. Because of the potential for intraindividual correlation among dietary exposures to all of the members of these two classes of contaminants, simply summing contaminant-specific exposure distributions to estimate the total exposure to these contaminant classes is likely to produce greater underestimates of exposure for individuals in the upper end of the joint exposure distribution than that observed in this simple example.

Conclusions

Food consumption data collected as part of two large prospective epidemiologic studies and contaminant residue data collected as part of the FDA Total Diet Study were combined to estimate the distribution of average daily dietary exposures to 11 food contaminants for a large population of U.S. adult males and females. The estimated distributions of dietary exposures were shown to be comparable to point estimates made by other researchers, indicating that the food frequency questionnaire-based approach produces reasonable results. Exposures were estimated to be highly variable among individuals, spanning two to three orders of magnitude, indicating that it is important to examine the range of dietary exposures when considering the public health risks of food contaminants. Intraindividual exposures to the 11 contaminants were estimated to be strongly correlated, which has implications for assessing the full public health impacts of exposures to contaminants that have the same toxicological effect.

For all of the chemicals included in our analysis, except heptachlor epoxide, exposures estimated at the upper end of the respective distributions were due to consumption of food items that contained measurable levels of the contaminant; that is, relatively reliable residue concentrations. This finding suggests that it may be possi-

ble to use dietary exposures estimated from diet questionnaires in epidemiological studies. The correlation coefficients presented earlier suggest that a principal components or factor analysis may reveal types or groups of food items that together determine the approximate level of an individual's exposure to compounds with similar toxicological action, which could also be used in epidemiological studies. Prior to such analyses, we recommend that a statistically designed study be conducted to validate these estimates by comparing biological indicators of exposure to the estimated exposures.

The estimated exposure distributions for some of the compounds were shown to be sensitive to valuation of the nondetect residue samples because of the low detection rate observed in the Total Diet Study data for these chemicals. We selected the 11 contaminants considered in this analysis based on their relatively high detection rates in the Total Diet Studies conducted from 1986 to 1991; thus, most other contaminants were detected less frequently. It can be inferred that estimates of dietary exposures to many other food contaminants will also be sensitive to the treatment of nondetect samples and the determinants of dietary exposure to these contaminants may not be readily identifiable. Therefore, we recommend that new monitoring studies be conducted that use a study design more sensitive than that employed by the Total Diet Study. In addition, we recommend that population-based estimates of exposures to contaminants in food be conducted for other subgroups of the United States, such as children and ethnic populations.

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